recite a method for generating a culture of purified or enriched neural progenitor cells. Applicants have further amended claims 42 and 44-49 to recite pluripotential cells in place of multipotential cells. Support for this amendment can be found throughout the specification, including the claims as filed and page 1, paragraph 1 of the specification. None of the amendments introduce new matter.

The Examiner has objected to the amendment of the specification incorporating the priority application (Serial No. PCT/GB99/01136) by reference, as allegedly adding new matter to the application. Applicants disagree for at least two reasons.

First, the amendment to the specification identifying the priority claim was not filed on April 1, 2002, as alleged by the Examiner. It was filed together with the application on October 12, 2002. (A copy of the application transmittal papers, which contained this amendment, was provided as a courtesy to the Examiner on April 1, 2002.) Because the amendment was part of the application as filed, it cannot be considered new matter. Further, the application filed on October 12, 2000, is identical to priority application Serial No. PCT/GB99/01136. As a result, it is not possible for this incorporation by reference to add new matter. However, to facilitate prosecution, Applicants have amended the specification to eliminate the phrase "incorporated herein by reference." Applicants request that the rejection be withdrawn.

Claims 42-54, 58, 64, and 65 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner contends that the term "multipotential cell" is vague and that "it is unclear as to the metes and bounds of what would be considered 'multipotential cell.'" The Examiner provided a copy of a document published by the National Institutes of Health (Stem cells: A Primer, http://www.nih.gov/news/stemcell/primer.htm, May 2000) which discusses the difference

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between pluripotent and multipotent cells. The documents states that pluripotent cells can form "virtually all of the tissues of the human body" (e.g., embryonic stem cells) whereas multipotent cells are pluripotent stem cells that have undergone "further specialization into stem cells that are committed to give rise to cells that have a particular function," such as blood stem cells.

The claims are directed to a method of generating a culture of cells purified or enrighed in neural progenitor cells, i.e., multipotential cells. Therefore, it is evident the starting cells must be pluripotential. In an effort to render the claims more clear, applicants have amended claims 42, 44-49 to recite pluripotential cells in place of multipotential cells. Applicants believe that the amended claims are now sufficiently definite and request that the Examiner withdraw the rejection of the claims under 35 U.S.C. § 112, second paragraph.

Applicants respectfully submit that the claims are now in condition for allowance and request a timely issuance of a notice of allowance.

Applicants believe that any necessary extension of time is accounted for by the Petition for Extension filed concurrently with this response. However, in the event of an error, please grant any additional extensions of time required to enter this Amendment and Response and charge any additional required fees to deposit account 06-0916.

Respectfully submitted,

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Dated: Oct. 7, 2002

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AMENDMENTS WITH CHANGES SHOWN

Amendment to the Specification at page 1:

This is a continuation of application Serial No. PCT/GB99/01136, filed April 14, 1999[, which is incorporated herein by reference].

Claim Amendments:

42. (Amended) A method for generating a culture that is purified or enriched in neural progenitor cells [respect of cells of a selected lineage], comprising:

(i) introducing into a pluripotential [multipotential] cell a selectable marker that is differentially expressed in neural progenitor cells [of the selected lineage] compared with its expression in other cells, wherein neural progenitor cells [of the selected linage] constitute a sub-set of the cells obtainable from the pluripotential [multipotential] cell;

(ii) culturing the pluripotential [multipotential] cell *in vitro* to induce differentiation of the pluripotential [multipotential] cell into a neural progenitor cell [of the selected lineage] or into a mixture of cells including neural progenitor cells [of the selected lineage], or to induce preferential survival, in a mixed culture of cells, of neural progenitor cells [of the selected lineage]; and

(iii) selecting for neural progenitor cells [of the selected lineage] according to differential expression of the selectable marker introduced in step (i).

44. (Amended) A method according to Claim 42 wherein the pluripotential [multipotential] cell is selected from embryonic stem (ES) cells, embryonic germ (EG) cells, embryonic carcinoma (EC) cells, a primary culture of fetal cells, a primary culture of post-natal cells, and a primary culture of adult cells.

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45. (Amended) A method according to Claim 42 comprising genetically modifying pluripotential [multipotential] cells to delete, mutate, substitute or add genes in order (i) to assay gene function in neural progenitor [cells of the selected lineage], and/or (ii) to render selected cells more suitable for transplantation.

46. (Amended) A method according to [any of] Claim 42 further comprising:-

(iv) introducing into the pluripotential [multipotential] cell a second selectable marker that is differentially expressed in cells of a selected sub-lineage compared with its expression in other cells, wherein cells of the selected sub-lineage are formed by differentiation of neural progenitor cells [of the selected progenitor lineage]; and

(v) when a culture of neural progenitor cells [of the selected lineage] has been obtained, allowing or inducing differentiation of the cells and selecting for cells that express the second selectable marker.

47. (Twice Amended) A method according to Claim 42 wherein the selectable marker is introduced into the pluripotential [multipotential] cell by targeted integration or random gene trap integration so as to be operatively coupled to a gene that is differentially expressed in neural progenitor cells [of the selected lineage].

48. (Twice Amended) A method according to Claim 42 wherein the selectable marker is introduced into the pluripotential [multipotential] cell via random integration of a transgene in which the selectable marker is operatively coupled to a gene that is differentially expressed in neural progenitor cells [of the selected lineage].

49. (Twice Amended) A method according to Claim 42 wherein the pluripotential [multipotential] cell is an ES, EG, or EC cell and the method comprises forming an embryoid body, or otherwise inducing differentiation of the cells.

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50. A method according to Claim 49 wherein the differentiated cells are dissociated so as to form a culture comprising of individual cells.

51. A method according to Claim 49 wherein differentiated cells of an embryoid body are dissociated using a protease, such as trypsin.

53. A method according to Claim 42 [Claim 52] wherein the selectable marker is expressed in cells that express a Sox gene.

54. A method according to Claim 53 wherein the Sox gene is selected from Sox 1, Sox 2 and Sox 3.

58. A method according to Claim 42 wherein the selectable marker is an antibiotic resistance gene and the method comprises culture in the presence of antibiotic.

64. A method of preparing a neural progenitor cell or a differentiated progeny thereof for storage, comprising obtaining the cell in a method according to Claim 42 and freezing the cell in the presence of a cryoprotectant.

65. A method of generating purified neurons, comprising obtaining a culture purified in respect of neural progenitors, using the method of Claim 42 wherein the selectable marker is differentially expressed in cells that express a Sox gene, and culturing the progenitors obtained in the presence of medium suitable for differentiation of the progenitor into neurons.

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